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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/458,299	12/10/1999	JOHN FIKES	18623-014800	8698

26111 7590 06/22/2004

STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 06/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/458,299	FIKES ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/2/03, 7/12/02, 9/17/01 and 2/23/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41-92* is/are pending in the application.

4a) Of the above claim(s) *76-92* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *both 3/21/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments filed 9/2/03, 7/12/02 and 9/17/01 and Applicant's response filed 2/23/04 are acknowledged and have been entered.

2. Applicant's election without traverse of the species of peptide SEQ ID NO: 4233 KVFGSLAFV in Applicant's response filed 9/2/03 and species of 9 amino acid residues in length, a fusion heteropolymer comprising the said peptide and composition thereof in Applicant's response filed 2/23/04 is acknowledged.

With regard to the election of the aforementioned later three species, because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement for the latter three species, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 41-75 read on the elected species, SEQ ID NO: 4233.

Accordingly, claims 76-92 (non-elected species of Group I) are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 41-75 are currently being examined.

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The declaration is defective because: the declaration claims priority under 35 USC section 120 to numerous applications that have been deleted from the first line of the specification in Applicant's amendment filed 9/2/03 and the first line of the specification claims priority to provisional application 60/141,422 that is not listed in the declaration.

4. The disclosure is objected to because of the following informalities:

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on page 16 at line 7. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 49, 54-58, 68, 69, 71 and 75 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the Applicant had possession at the time of invention of the claimed peptide/ composition thereof comprising SEQ ID NO: 4233 or SEQ ID NO: 4239 and/or further comprising one or more different peptides that are not Th epitope peptides or TAA (tumor associated antigen) peptides, or a peptide of 9, 10 or 11 amino acid residues in length comprising SEQ ID NO: 4233 or SEQ ID NO: 4239 linked to a lipid that is not P3CSS.

The instant claims encompass peptides/compositions thereof comprising SEQ ID NO: 4233 or SEQ ID NO: 4239 and *any* other peptide(s) or *any* other amino acid residues on either the N- or C-terminus of the peptide up to any length. There is insufficient disclosure in the specification such compositions comprising other peptides that are not Th epitope peptides or TAA peptides (CTL epitopes) or peptides that induce antibody production to elicit immunity for the same tumor targets or flanking amino acid residues that are not portions of the protein from which the peptides derive, i.e., the Her-2/neu protein.

The instant specification discloses Her-2/neu peptides linked to carriers or linked as homopolymers or heteropolymers, and where different peptide epitopes are used to make up the polymer, and the ability to induce antibodies and/or CTLs that react with different antigenic determinants of the tumor-related peptide targeted for an immune response (last paragraph on page 42).

There is no disclosure of compositions comprising other peptides that are not Th epitope peptides or TAA CTL epitope peptides, or flanking sequences from the Her-2/neu protein. One of ordinary skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

7. Claims 49, 54-58, 68, 69, 71 and 75 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected to make and/or use the invention.

The specification does not disclose how make and or/use a composition comprising SEQ ID NO: 4233 or SEQ ID NO: 4239 and further comprising one or more different peptides that are not Th epitope peptides or TAA (tumor associated antigen) peptides, or flanking amino acid residues that are not portions of the protein from which the peptides derive, i.e., the Her-2/neu protein.

The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass compositions comprising SEQ ID NO: 4233 or SEQ ID NO: 4239 and *any* other peptide(s) or any other flanking amino acid sequences.

The instant specification discloses her-2/neu peptides linked to carriers or linked as homopolymers or heteropolymers, and where different peptide epitopes are used to make up the polymer, the additional ability to induce antibodies and/or CTLs that react with different antigenic determinants of the tumor-related peptide targeted for an immune response (last paragraph on page 42).

Evidentiary reference Shastri et al (J. Immunol. 155: 4339-4346, 11/1995, Applicant's IDS reference) teaches that presentation of endogenous peptide/MHC class I complexes is profoundly influenced by specific C-terminal flanking residues and that the peptides are precisely cleaved products. Evidentiary reference Eisenlohr et al (J. Exp. Med. 175: 481-487, 2/1992, Applicant's IDS reference) teaches that CTL recognize peptides of 8-10 amino acid residues complexed with MHC class I molecules and that flanking residues can influence the presentation of peptide antigens to CTL.

There is insufficient disclosure in the specification such compositions comprising other peptides that are not Th epitope peptides or TAA peptides (CTL epitopes) or peptides that induce antibody production to elicit immunity for the same tumor target, or flanking amino acid residues that are not portions of the protein from which the peptides derive, i.e., the Her-2/neu protein. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 45-48 and 63-68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 45 and 63 are indefinite in the recitation of "The peptide of claim 41, which is fused to a T helper epitope" because it is not clear what is meant. The peptide recited in claim 41 is 9, 10 or 11 amino acid residues in length, not the length for a fusion protein consisting of the peptide of claim 41 linked to a t helper peptide.

b. Claim 46 is indefinite in the recitation of "The peptide of claim 41, which is fused to spacer or linker amino acids" because it is not clear what is meant. The peptide recited in claim 41 is 9, 10 or 11 amino acid residues in length, and it is not clear how a peptide consisting of 9 amino acid residues can be linked to any spacer or amino acid residues and still consist of 9 amino acid residues.

c. Claims 47 and 67 are indefinite in the recitation of "The peptide...which is fused to a carrier" because the peptides recited in base claims 41 and 59, respectively, are 9, 10 or 11 amino acid residues in length, not the length for a fusion protein consisting of the peptide of claim 41 or 59, respectively, fused to a carrier.

d. Claims 48 and 68 are indefinite in the recitation of "The peptide...which is linked to a lipid" because it is not clear what is meant. The peptides recited in the base claims 41 and 59, respectively, are 9, 10 or 11 amino acid residues in length. It is suggested that Applicant amend the said claim if a composition comprising a peptide linked to a lipid is meant.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 41, 44, 54, 58, 59, 62, 72, 74 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawashima et al (Human Immunology 59, 1-14, 1/1998, Applicant's IDS reference) in view of Sidney et al (Immunology Today 17(6), 261-266, 1996) and Rowland-Jones (J. Clin. Invest. 102(9), 1758-1765, 11/1998).

Kawashima et al teach the Her2[369] peptide epitope KIFGSLAFL that binds to HLA-A2 supertype motif alleles (especially Table 4 and Table 3 and page 6 at the last paragraph and continuing onto page 7 through the paragraph spanning columns 1 and 2). Kawashima et al further teach that the said peptide epitope binds with low affinity to HLA-A*6802 (especially Table 4). Kawashima et al teach the high frequency of HLA-A*6802 in the black population (especially paragraph spanning pages 7 and 8). Kawashima et al teach cocktails of the peptide with other peptides and pharmaceutical carriers (especially last paragraph).

Kawashima et al do not teach the peptide KVFGSLAFV (SEQ ID NO: 4233 of the instant application).

Sidney et al teach the A2-like binding supertype alleles include the HLA alleles listed in Table 4 of Kawashima et al, and in addition include HLA-A*6901 among others listed in Table 3 of Sidney et al. Sidney et al further teach the supermotif for binding to the HLA-A2-like alleles is AILMVT at position two of the peptide for binding of the side chain of the P2 amino acid residue in the B pocket of HLA and AILMVT at the carboxy-terminus of the peptide for binding of the side chain of the carboxy-terminal amino acid residue in the F pocket of HLA (especially Table 4). Sidney et al teach the advantage of using epitopes that bind to supertype alleles for greater coverage in populations (especially page 261 at the paragraph spanning columns 1 and 2).

Rowland-Jones et al teach use of a VT at P2 and VL at P9 motif for predicting peptides that bind to HLA-A*6802 (especially page 1759 at the second full paragraph).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have altered the Her2[9369] peptide epitope KIFGSLAFL taught by Kawashima et al by substituting a V at position 2 and a V at position 9 (i.e., to produce the peptide KVFGSLAFV, SEQ ID NO: 4233 of the instant application and pharmaceutical composition thereof) as taught by Rowland-Jones et al for peptides that bind to the HLA-A2-like supertype allele HLA-A*6802 taught by Sidney et al or for peptides that bind to HLA-A2-like supertype alleles as taught by Sidney et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a peptide that would bind with higher affinity to HLA-A*6802 the allele that is present in high frequency in the black population as taught by Kawashimi et al because Kawashima et al teach a peptide epitope KIFGSLAFL that binds to HLA-A*6802 with low affinity and Sidney et al teach the supermotif for binding to HLA-A2-like alleles (which

includes HLA-A*6802) includes a V at position 2 and position 9 and Rowland-Jones et al teaches V at position 2 and 9 for binding to HLA-A*6802.

12. Claims 41, 44, 54, 58, 59, 62, 74 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lustergarten et al (Human Immunology 52, 109-118, 2/1997, Applicant's IDS reference) in view of Rowland-Jones et al (J. Clin. Invest. 102(9), 1758-1765, 11/1998).

Lustergarten et al teach the immunogenic HLA-A2.1 binding peptide p369, KIFGSLAFL, from Her-2/neu tumor antigen [369] (especially Table 1). Lustergarten et al teach the consensus motif for peptide binding to HLA-A2.1 is LIMVAT at position 2 and LIMVAT at the carboxy-terminal position (especially Results section). Lustergarten et al teach compositions comprising the said peptide and pharmaceutical carriers. Lustergarten et al teach targeting of
Her-2/neu for immunotherapy (especially abstract). Lustergarten et al teach a second immunogenic peptide, p773, a 10-mer peptide from Her-2/neu tumor antigen that has a V at position 10 (Table 1 and results and discussion sections). Lustergarten et al also teach use of T helper epitopes with the aforementioned [CTL] epitope peptides (especially page 116 at the last sentence of column 1).

Lustergarten et al do not teach the peptide KVFGSLAFV (SEQ ID NO: 4233 of the instant application).

Rowland-Jones et al teach use of a VT at P2 and VL at P9 motif for predicting peptides that bind to HLA-A*6802 (especially page 1759 at the second full paragraph), and further teach the presence of a supermotif that comprises some HLA-A2 subtypes such as A*201 and A*6802 (especially column 1 on page 1764).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have altered the Her2[369] peptide epitope KIFGSLAFL taught by Lustergarten et al by substituting a V at position 2 and a V at position 9 (i.e., to produce the peptide KVFGSLAFV, SEQ ID NO: 4233 of the instant application and pharmaceutical composition thereof) as taught by Rowland-Jones et al for peptides that bind to the HLA-A2-like supertype allele HLA-A*6802 taught by Rowland-Jones et al. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have also altered the p773 peptide taught by Lustergarten for binding to HLA-A*6802 as taught by Rowland-Jones et al for use of both Her2/neu peptides together.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make an immunogenic peptide that would bind to HLA-A*6802/composition thereof for administration to HLA-A*6802 positive Her2/neu tumor positive individuals because Lustergarten et al teaches a peptide epitope KIFGSLAFL and another p773 that binds to HLA-A2.1 and is useful for immunotherapeutic targeting of

Her2/neu positive tumors and Rowland-Jones et al teaches V at position 2 and 9 for binding to HLA-A*6802.

13. Claims 42, 43, 45-53, 55-57, 60, 61, 63-71 and 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawashima et al (Human Immunology 59, 1-14, 1/1998, Applicant's IDS reference) in view of Sidney et al (Immunology Today 17(6), 261-266, 1996) and Rowland-Jones (J. Clin. Invest. 102(9), 1758-1765, 11/1998) as applied to claims 41, 44, 54, 58, 59, 62, 72, 74 and 75 above and further in view of WO 95/19783A1.

Kawashima et al teach the Her2[369] peptide epitope KIFGSLAFL that binds to HLA-A2 supertype motif alleles (especially Table 4 and Table 3 and page 6 at the last paragraph and continuing onto page 7 through the paragraph spanning columns 1 and 2). Kawashima et al further teach that the said peptide epitope binds with low affinity to HLA-A*6802 (especially Table 4). Kawashima et al teach the high frequency of HLA-A*6802 in the black population (especially paragraph spanning pages 7 and 8). Kawashima et al teach cocktails of the peptide with other peptides and pharmaceutical carriers (especially last paragraph).

Kawashima et al do not teach the peptide KVFGSLAFV (SEQ ID NO: 4233 of the instant application).

Sidney et al teach the A2-like binding supertype alleles include the HLA alleles listed in Table 4 of Kawashima et al, and in addition include HLA-A*6901 among others listed in Table 3 of Sidney et al. Sidney et al further teach the supermotif for binding to the HLA-A2-like alleles is AILMVT at position two of the peptide for binding of the side chain of the P2 amino acid residue in the B pocket of HLA and AILMVT at the carboxy-terminus of the peptide for binding of the side chain of the carboxy-terminal amino acid residue in the F pocket of HLA (especially Table 4). Sidney et al teach the advantage of using epitopes that bind to supertype alleles for greater coverage in populations (especially page 261 at the paragraph spanning columns 1 and 2).

Rowland-Jones et al teach use of a VT at P2 and VL at P9 motif for predicting peptides that bind to HLA-A*6802 (especially page 1759 at the second full paragraph).

WO 95/19783A1 teaches the universal Th (T helper) peptide aKSVWANTLKAAa (SEQ ID NO: 4226 of the instant claim 65) (especially claim 21 and the paragraph spanning pages 14 and 15) linked to an immunogenic peptide. WO 95/19783A1 further teaches an immunogenic peptide/pharmaceutical compositions thereof linked to a lipidated peptide, or to Th epitopes or to carriers in order to increase immunogenicity of a peptide, and wherein spacer or linker amino acid residues are added (especially claims 18 and 19, page 13 at paragraph 1 and 2, page 14, and page 8 at paragraph 3). WO 95/19783A1 teaches that the peptides are between about 8 and about 20 residues, preferably 9 or 10. WO 95/19783A1 teaches substituted peptides for change in function such as affinity of binding to MHC or to TCR (especially page 12). WO 95/19783A1 also teaches fusion proteins comprising one or more immunogenic

peptides (especially pages 16 at the third paragraph) and pharmaceutical compositions thereof (especially page 19) and administration via liposomes (especially pages 19 and 20). WO 95/19783A1 teaches homo or heteropolymers of the said immunogenic peptides/compositions thereof (especially page 21 at paragraph 2).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have altered the Her2[369] peptide epitope KIFGSLAFL taught by Kawashima et al by substituting a V at position 2 and a V at position 9 (i.e., to produce the peptide KVFGSLAFV, SEQ ID NO: 4233 of the instant application and pharmaceutical composition thereof) as taught by Rowland-Jones et al for peptides that bind to the HLA-A2-like supertype allele HLA-A*6802 taught by Sidney et al or for peptides that bind to HLA-A2-like supertype alleles as taught by Sidney et al. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have fused the peptide(s) to a Th peptide such as the universal Th peptide epitope taught by WO 95/19783A1 as taught by WO 95/19783A1 for other immunogenic CTL epitope peptides, to have fused the peptide(s) to linker amino acid residues and to a carrier or link it to a lipid or to administer it via a liposome, or to make it as a homo or heteropolymer or a composition comprising more than one immunogenic peptide as taught by WO 95/19783A1 for other immunogenic peptides.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a peptide that would bind with higher affinity to HLA-A*6802 the allele that is present in high frequency in the black population as taught by Kawashimi et al because Kawashima et al teach a peptide epitope KIFGSLAFL that binds to HLA-A*6802 with low affinity and Sidney et al teach the supermotif for binding to HLA-A2-like alleles (which includes HLA-A*6802) includes a V at position 2 and position 9 and Rowland-Jones et al teaches V at position 2 and 9 for binding to HLA-A*6802. One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a more effective peptide composition capable of stimulating an immune response, as taught for the fusion peptides, or lipid linked peptides or liposome administered peptides taught by WO 95/19783A1. Claims 42, 43, 60 and 61 are included in this rejection because it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made a peptide of 10 or 11 amino acid residues comprising the 9-mer epitope because WO 95/19783A1 teaches peptides between about 8 and about 20 amino acid residues long comprising the immunogenic motif-bearing peptides.

14. Claims 42, 43, 45-53, 55-57, 60, 61, 63-71 and 73 are rejected under 35 U.S.C. 103(a) as being obvious over Lustergarten et al (Human Immunology 52, 109-118, 2/1997, Applicant's IDS reference) in view of Rowland-Jones et al (J. Clin. Invest. 102(9), 1758-1765, 11/1998) as applied to claims 41, 44, 54, 58, 59, 62, 72, 74 and 75 above and further in view of WO 95/19783A1.

Lustergarten et al teach the immunogenic HLA-A2.1 binding peptide p369, KIFGSLAFL, from Her-2/neu tumor antigen (especially Table 1). Lustergarten et al teach the consensus motif for peptide binding to HLA-A2.1 is LIMVAT at position 2 and LIMVAT at the carboxy-terminal position (especially Results section). Lustergarten et al teach compositions comprising the said peptide and pharmaceutical carriers. Lustergarten et al teach targeting of Her-2/neu for immunotherapy (especially abstract). Lustergarten et al teach a second immunogenic peptide, p773, a 10-mer peptide from Her-2/neu tumor antigen that has a V at position 10 (Table 1 and results and discussion sections). Lustergarten et al also teach use of T helper epitopes with the aforementioned [CTL] epitope peptides (especially page 116 at the last sentence of column 1).

Lustergarten et al do not teach the peptide KVFGSLAFV (SEQ ID NO: 4233 of the instant application).

Rowland-Jones et al teach use of a VT at P2 and VL at P9 motif for predicting peptides that bind to HLA-A*6802 (especially page 1759 at the second full paragraph), and further teach the presence of a supermotif that comprises some HLA-A2 subtypes such as A*201 and A*6802 (especially column 1 on page 1764).

WO 95/19783A1 teaches the universal Th (T helper) peptide aKSVWANTLKAAa (SEQ ID NO: 4226 of the instant claim 65) (especially claim 21 and the paragraph spanning pages 14 and 15) linked to an immunogenic peptide. WO 95/19783A1 further teaches an immunogenic peptide/pharmaceutical compositions thereof linked to a lipidated peptide, or to Th epitopes or to carriers in order to increase immunogenicity of a peptide, and wherein spacer or linker amino acid residues are added (especially claims 18 and 19, page 13 at paragraph 1 and 2, page 14, and page 8 at paragraph 3). WO 95/19783A1 teaches that the peptides are between about 8 and about 20 residues, preferably 9 or 10. WO 95/19783A1 teaches substituted peptides for change in function such as affinity of binding to MHC or to TCR (especially page 12). WO 95/19783A1 also teaches fusion proteins comprising one or more immunogenic peptides (especially pages 16 at the third paragraph) and pharmaceutical compositions thereof (especially page 19) and administration via liposomes (especially pages 19 and 20). WO 95/19783A1 teaches homo or heteropolymers of the said immunogenic peptides/compositions thereof (especially page 21 at paragraph 2).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have altered the Her2[9369] peptide epitope KIFGSLAFL taught by Lustergarten et al by substituting a V at position 2 and a V at position 9 (i.e., to produce the peptide KVFGSLAFV, SEQ ID NO: 4233 of the instant application and pharmaceutical composition thereof) as taught by Rowland-Jones et al for peptides that bind to the HLA-A2-like supertype allele HLA-A*6802 taught by Rowland-Jones et al. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have also altered the 773 peptide taught by Lustergarten for binding to HLA-A*6802 as taught by Rowland-Jones et al for use of both Her2/neu peptides together. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have fused the peptide(s) taught by the combination of Lustergarten et al and Rowland-Jones et al to a Th peptide such as the universal Th peptide epitope as taught by WO 95/19783A1 for other immunogenic CTL epitope peptides, to have fused the peptide(s) to linker amino acid residues and to a carrier or link it to a lipid or to administer it via a liposome, or to make it as a homo or heteropolymer or a composition comprising more than one immunogenic peptide as taught by WO 95/19783A1 for other immunogenic peptides.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make an immunogenic peptide that would bind to HLA-A*6802/composition thereof for administration to HLA-A*6802 positive Her2/neu tumor positive individuals because Lustergarten et al teaches a peptide epitope KIFGSLAFL and another 773 that binds to HLA-A2.1 and is useful for immunotherapeutic targeting of Her2/neu positive tumors and Rowland-Jones et al teaches V at position 2 and 9 for binding to HLA-A*6802. One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make a more effective peptide composition capable of stimulating an immune response, as taught for the fusion peptides, or lipid linked peptides or liposome administered peptides taught by WO 95/19783A1. Claims 42, 43, 60 and 61 are included in this rejection because it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made a peptide of 10 or 11 amino acid residues comprising the 9-mer epitope because WO 95/19783A1 teaches peptides between about 8 and about 20 amino acid residues long comprising the immunogenic motif-bearing peptides.

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 41-75 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 and 15-27 of copending Application No.US2004/0018971 A1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending Application No.US2004/0018971 A1 discloses that peptides of the invention can be from 8 to 11 amino acid residues in length (page 14, paragraph 0162), SEQ ID NO: 4233 of the instant application is in Table XXVII of the Application No.US2004/0018971 A1, and the SEQ ID NO: 4226 universal T helper epitope of instant claim 65 is a HTL epitope disclosed in Application No.US2004/0018971 A1 (on page 20 at paragraph 0219).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

17. Claims 41-75 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 6-13, 18-31 and 35-38 of copending Application No.US2003/0224036 A1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending Application No. US2003/0224036 A1 discloses that peptides of the invention can be from about 8 to about 13 amino acid residues in length (page 6, paragraph 0049), and the SEQ ID NO: 4226 universal T helper epitope of instant claim 65 is a HTL epitope disclosed in Application No. US2003/0224036 A1 on page 18 at paragraph 0180).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

18. The references AR30 and AS25 crossed out in the Forms 1449 filed 3/21/03 have not been considered because they have not been provided by Applicant. Reference AM1 has not been considered because no translation has been provided.

19. No claim is allowed.

20. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware of in the specification.

21. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Wednesday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Chan Y Christina, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640
Technology Center 1600
June 18, 2004

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600